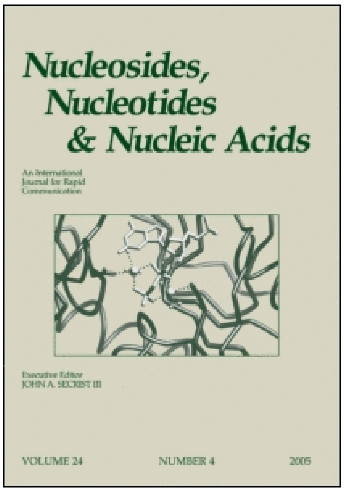

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REACTIONS OF 2'-DEOXY-2'-HALOURIDINES AND O^2,2'-CYCLOURIDINE WITH LITHIUM DIALKYLAMIDES: FORMATION OF 1',2'-UNSATURATED DERIVATIVES

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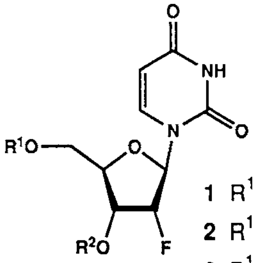
Abstract: Treatment of 2'-deoxy-2'-halouridine derivatives with lithium diisopropylamide (LDA) resulted in partial formation of the 1',2'-unsaturated nucleosides, no lithiation being observed in the base moiety of the recovered starting material. Reactions of an O^2,2'-cyclouridine derivative with LDA or lithium 2,2,6,6-tetramethylpiperidide (LTMP) were also examined.

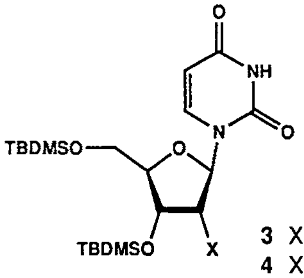
Lithiation of nucleosides has now a firm place as a highly general method for the modification of the base moiety,1) since a variety of analogues can be readily synthesized from a common lithiated species simply by changing electrophiles used. Our study on the C-6 lithiation of 5-substituted 2',3'-*O*-isopropylidene-5'-*O*-methoxymethyluridine derivatives shows that all 5-halogeno substituents (-F, -Cl, -Br, and -I) remain intact under the reaction conditions, wherein lithium diisopropylamide (LDA) was used as a lithiating agent: neither aryne formation nor halogen-lithium exchange was observed.2) On the other hand, when a 6-iodouridine derivative prepared by the above method was used as a substrate, halogen-lithium exchange becomes a dominant reaction path even by the use of LDA.3) In contrast to these available evidence concerning compatibility of halogeno substituents in the base moiety, no such information has so far been disclosed for those in the sugar portion of nucleosides.

Nucleosides bearing a fluorine-substituted sugar structure[4)] have attracted considerable interests due to their possible biological activities. We recently reported on the use of diethylaminosulfur trifluoride (DAST) in the fluorodehydroxylation of pyrimidine nucleosides having a 2',3'-vicinal diol system.[5)] 2'-Deoxy-2'-fluorouridine (**1**) can be readily prepared by this method. We intended to synthesize 6-substituted derivatives of **1** by means of lithiation. In this paper, the results of some experiments initiated with the above motivation are described.

The 3'- and 5'-hydroxyls of **1** were protected with *tert*-butyldimethylsilyl (TBDMS) groups, which have been known to be stable under lithiation conditions, to give **2** in quantitative yield. 2'-Chloro (**3**) and 2'-bromo (**4**) counterparts were also prepared by silylation of the corresponding free nucleoside.[6)] When **2** was treated with 3 equiv. of LDA in THF below -70 °C for 15 min and then reacted with CH_3OD, a product was isolated in addition to the recovered **2** (25%). The ^{1}H-NMR spectrum of this product was devoid of H-1' and a signal attributable to H-2' was observed as a doublet (J= 2.9 Hz). Together with its UV spectrum, which has a maximum absorption at a significantly longer wavelength of 275 nm in MeOH, the structure of this product was determined to be 1-(3,5-bis-*O*-TBDMS-2-deoxy-D-*erythro*-pent-1-enofuranosyl)uracil (**5**).[7)] Its MS spectrum and elemental analysis were also in accord with the structure. The yield was 33%. It should be noted that similar treatment of **3** or **4** with LDA resulted in recovery of a larger amount of the starting material (**3**; 59%, **4**; 64%).

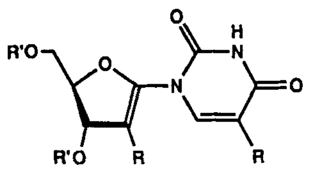


1 $R^1 = R^2 = H$
2 $R^1 = R^2 =$ TBDMS
6 $R^1 =$ TBDMS, $R^2 = H$

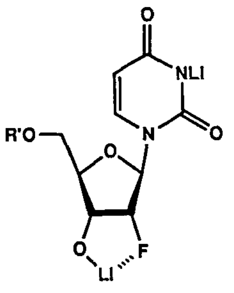


3 X= Cl
4 X= Br

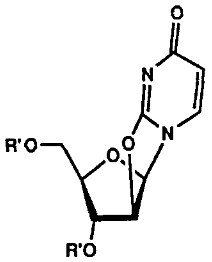
Examination of the ^{1}H-NMR spectra of **5** and the recovered **2** in $CDCl_3$ showed that the C-6 position of the former[8)] had been deuterated to the extent of 79% whereas no deuterium incorporation had taken place in the case of the latter. Our previous study indicates that protection of uridine with 2',3'-*O*-isopropylidene group provides a certain advantage for LDA to lithiate the C-6 position.[9] This led us



5 R= H, R'= TBDMS
9 R= TMS, R'= TBDMS



7 R'= TBDMS



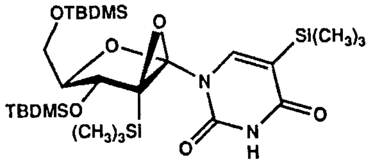
8 R'= TBDMS

to choose **6** as a substrate with the expectation that an intermediate depicted as **7** could be formed.[10] Although the occurrence of the elimination pathway was prevented by using **6** (5 equiv. of LDA), the recovered **6** (recovery 95%) was found again not to contain deuterium to any detectable extent.

To obtain mechanistic evidence of the reaction of **2** forming **5**, O^2,2'-cyclouridine derivative **8**[7] was reacted with LDA (3.5 equiv.) and then quenched with CH_3OD. Acidification with AcOH followed by column chromatography of the reaction mixture gave **5** in 54% yield as the sole product with a much the same level of deuteration at the C-6 position (74%). Although the aforementioned reaction of **2** with LDA had been carried out at the low temperature and a fluorine substituent is generally known to be a poor leaving group, the above experimental results of **8** suggest that the formation of **5** from **2** would occur *via* an intramolecular substitution to form **8** and subsequent abstraction of H-1'.[11]

A similar experiment of **8** using a more basic lithiating agent, lithium 2,2,6,6-tetramethylpiperidide[12] (LTMP, 3.5 equiv.), gave **5** in a slightly higher yield of 62%. As can be anticipated from a Lewis acid character of LTMP,[13] fairly different regioselectivity was observed in this case, the preferential site of deuteration being the C-5 position (D-5 42% *vs.* D-6 33%).

Finally, an additional experiment between **8** and LTMP was carried out in the presence of trimethylchlorosilane (TMSCl, 10



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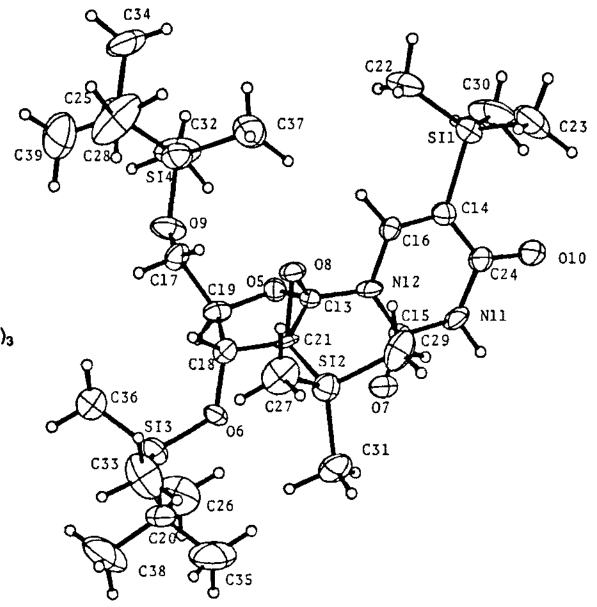

FIG. 1. ORTEP Drawing of Compound **10**.

equiv.) as an electrophilic trap.[14] Quite unexpectedly, the main product obtained in this reaction was found to contain two TMS groups. On the basis of its ^{1}H-NMR spectrum, the structure of this product was determined as **9** (77% yield).[15] At the present time, introduction of TMS group into the 2'-position is mechanistically unclear.[16] The presence of 2'-C-TMS group was further confirmed by X-ray crystallographic analysis of the corresponding 1',2'-epoxide **10**,[17] which was prepared in 64% yield by treatment of **9** with MCPBA (1.0 equiv.) in CH_2Cl_2.[18] An ORTEP drawing of **10** is depicted in Figure 1 and atomic coordinates and thermal parameters used for the analysis are listed in Table 1.

EXPERIMENTAL

All melting points were determined with a Yanagimoto micro-melting point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on either a JEOL JNM-FX 100 or a JEOL GX-400 spectrometer with tetramethylsilane as an internal standard. ^{13}C-NMR

TABLE 1. Atomic Coordinates and Isotropic Thermal Parameters of Non-hydrogen Atoms Used for Crystallographic Analysis of **10**.

Atom	X	Y	Z	B_{eq} (Å^2)
SI1	0.1071(2)	0.2521	0.6307(2)	5.24(14)
SI2	0.1102(2)	0.0049(9)	1.1519(3)	5.19(14)
SI3	0.3215(2)	-0.1580(10)	1.3367(3)	5.39(14)
SI4	0.3830(2)	-0.2752(11)	0.8424(3)	6.29(17)
O 5	0.2769(5)	0.0349(16)	0.9939(6)	4.08(29)
O 6	0.2778(4)	-0.0495(14)	1.2380(5)	3.94(26)
O 7	0.2003(6)	0.3986(16)	1.0681(7)	5.78(37)
O 8	0.1715(5)	-0.1242(15)	0.9859(6)	4.19(29)
O 9	0.3819(4)	-0.2279(20)	0.9621(6)	6.16(38)
O 10	0.1005(6)	0.6104(19)	0.7632(8)	6.92(41)
N 11	0.1501(7)	0.4985(21)	0.9155(10)	4.89(43)
N 12	0.1755(6)	0.1891(19)	0.9401(8)	4.26(39)
C 13	0.2097(8)	0.0454(23)	0.9981(10)	3.38(42)
C 14	0.1289(7)	0.2957(23)	0.7725(10)	4.24(48)
C 15	0.1785(7)	0.3643(27)	0.9820(12)	4.32(51)
C 16	0.1541(7)	0.1602(22)	0.8359(10)	3.61(46)
C 17	0.3274(9)	-0.2736(28)	1.0166(13)	4.81(53)
C 18	0.2538(7)	-0.1315(26)	1.1406(10)	4.02(47)
C 19	0.3065(7)	-0.1000(22)	1.0691(10)	4.02(44)
C 20	0.3657(10)	0.0284(33)	1.4170(12)	6.71(64)
C 21	0.1895(7)	-0.0365(21)	1.0921(9)	3.72(41)
C 22	0.1332(18)	0.0082(45)	0.6077(18)	7.56(97)
C 23	0.0139(13)	0.2911(52)	0.5893(17)	8.96(95)
C 24	0.1245(9)	0.4768(26)	0.8118(11)	5.07(54)
C 25	0.3966(12)	-0.5234(40)	0.8290(14)	8.80(84)
C 26	0.4077(19)	0.1481(50)	1.3546(27)	10.12(97)
C 27	0.0848(12)	-0.2298(36)	1.1827(20)	7.53(82)
C 28	0.3377(19)	-0.6390(41)	0.8647(45)	12.37(98)
C 29	0.0410(13)	0.1078(46)	1.0518(23)	8.17(93)
C 30	0.1582(27)	0.4201(60)	0.5675(22)	12.24(96)
C 31	0.1305(12)	0.1631(42)	1.2611(17)	8.00(91)
C 32	0.4555(13)	-0.1370(42)	0.8103(19)	8.64(92)
C 33	0.2609(15)	-0.2878(50)	1.4070(23)	9.31(98)
C 34	0.3954(23)	-0.5648(51)	0.7110(20)	10.42(97)
C 35	0.3120(20)	0.1563(59)	1.4495(25)	12.67(93)
C 36	0.3866(18)	-0.3178(46)	1.2963(23)	9.15(89)
C 37	0.2987(14)	-0.1927(53)	0.7648(19)	9.90(88)
C 38	0.4135(28)	-0.0451(80)	1.5114(26)	13.89(99)
C 39	0.4653(23)	-0.5766(57)	0.8874(34)	13.71(96)

spectrum of **10** in $CDCl_3$ was recorded on a JEOL GX-400 spectrometer with residual $CHCl_3$ (77.0 ppm) as a standard. Mass spectra (MS) were measured on a JEOL JMS-D 300 spectrometer. Ultraviolet (UV) spectra were recorded on a Shimadzu UV-240 spectrophotometer. THF was distilled from benzophenone ketyl. A commercially available hexane solution of BuLi was titrated before use with diphenylacetic acid in THF. TLC was performed on precoated silica gel plates F_{254}, Merck. Column chromatography was carried out on silica gel (Wakogel® C-200).

3',5'-Bis-*O*-TBDMS-2'-deoxy-2'-fluorouridine (2) TBDMSCl (251 mg, 1.7 mmol) was added to a solution of **1** (82 mg, 0.33 mmol) and imidazole (227 mg, 3.3 mmol) in DMF (4 ml). The mixture was stirred at room temperature for 16 h. After being diluted with EtOAc (30 ml), the reaction mixture was washed with water (3×5 ml) and then with brine (10 ml). The organic layer separated was dried (Na_2SO_4), evaporated, and chromatographed on a silica gel column (10~33% EtOAc/hexane). This afforded **2** (157 mg, 99%) as a solid. Crystallization from EtOAc-hexane gave an analytical sample (mp 163.0-163.5 °C). *Anal.* Calcd for $C_{21}H_{39}FN_2O_5Si_2$: C, 53.13; H, 8.28; F, 4.00; N, 5.90. Found: C, 52.94; H, 8.13; F, 3.90; N, 5.81. UV absorption in MeOH: max 259 nm (ε 10300), min 228 nm (ε 2600). ^1H-NMR ($CDCl_3$) δ: 0.10, 0.11, and 0.12 (12H, each as s, SiMe), 0.91 and 0.93 (18H, each as s, SiBu-*t*), 3.79 (1H, dd, *J*= 1.5 and 10.9 Hz, H-5'), 4.05 (1H, dd, *J*= 1.5 and 10.9 Hz, H-5'), 4.08 (1H, dt, *J*= 1.4 and 7.3 Hz, H-4'), 4.29 (1H, ddd, *J*= 4.0, 7.3, and 18.7 Hz, H-3'), 4.77 (1H, ddd, *J*= 1.8, 4.0, and 52.4 Hz, H-2'), 5.69 (1H, dd, *J*= 1.8 and 8.1 Hz, H-5), 6.06 (1H, dd, *J*= 1.8 and 15.4 Hz, H-1'), 7.92 (1H, d, J= 8.1 Hz, H-6), 8.78 (1H, br, NH). MS *m/z*: 417 (M^+–Bu-*t*), 345 (M^+–2Bu-*t*–Me), 303 (M^+–Bu-*t*–TBDMS).

3',5'-Bis-*O*-TBDMS-2'-chloro-2'-deoxyuridine (3) This compound was prepared from 2'-chloro-2'-deoxyuridine (2.41 g) as described in the preparation of **2**. Silica gel column chromatography (10~33% EtOAc/hexane) gave 2.44 g (54%) of **3** as a solid. Crystallization from EtOAc-hexane gave an analytical sample (mp 150.0-150.5 °C). *Anal.* Calcd for $C_{21}H_{39}O_5N_2ClSi_2$: C, 51.35; H, 8.00; N, 5.70. Found: C, 51.47; H, 8.25; N, 5.77. UV absorption in MeOH: max 258 nm (ε 10200), min 228 nm (ε 3100). ^1H-NMR ($CDCl_3$) δ: 0.11, 0.12, 0.13, and 0.14 (12H, each as s, SiMe), 0.92 and 0.94 (18H, each as s, SiBu-*t*), 3.76 (1H, dd, *J*= 1.8 and 11.9 Hz, H-5'), 3.98 (1H, dd, *J*= 2.6 and 11.9 Hz, H-5'), 4.12 (1H, ddd, *J*= 1.8, 2.6, and 4.5 Hz, H-4'), 4.20 (1H, t, *J*= 4.5 Hz, H-3'), 4.32 (1H, t, *J*= 4.8 Hz, H-2'), 5.70 (1H, dd, *J*= 1.8 and 8.3 Hz, H-5), 6.20 (1H, d, *J*= 4.8 Hz, H-1'), 7.88 (1H, d, *J*= 8.3 Hz, H-6), 8.76 (1H, br, NH). MS *m/z*: 435 (M^+–Bu-*t*+2), 433 (M^+–Bu-*t*).

3',5'-Bis-*O*-TBDMS-2'-bromo-2'-deoxyuridine (4) This compound was prepared from 2'-bromo-2'-deoxyuridine (599 mg) as described in the preparation of **2**. Silica gel column chromatography (10~33% EtOAc/hexane) gave 955 mg (92%) of **4** as a foam. *Anal.* Calcd. for $C_{21}H_{39}O_5N_2BrSi_2$: C, 47.09; H, 7.34; N, 5.23. Found: C, 47.36; H, 7.53; N, 5.08. UV absorption in MeOH: max 258 nm (ε 11000), min 229 nm (ε 3900). ^{1}H-NMR ($CDCl_3$) δ: 0.11, 0.12, 0.13, and 0.15 (12H, each as s, SiMe), 0.93 and 0.94 (18H, each as s, SiBu-*t*), 3.76 (1H, dd, J= 1.8 and 11.7 Hz, H-5'), 3.99 (1H, dd, J= 2.6 and 11.7 Hz, H-5'), 4.12 (1H, m, H-4'), 4.19 (1H, t, J= 4.8 Hz, H-3'), 4.24 (1H, t, J= 4.8 Hz, H-2'), 5.70 (1H, dd, J= 2.0 and 8.3 Hz, H-5), 6.26 (1H, d, J= 4.8 Hz, H-1'), 7.87 (1H, d, J= 8.3 Hz, H-6), 8.94 (1H, br, NH). MS *m/z*: 521 (M^+–Me+2), 519 (M^+–Me), 479 (M^+–Bu-*t*+2), 477 (M^+–Bu-*t*), 397 (M^+–Bu-*t*–HBr), 367 (M^+–B+2), 365 (M^+–B).

Lithiation and subsequent deuteration of 2'-deoxy-2'-halouridine derivatives (2~4, 6, and 8) These reactions were carried out in the same manner as the following example of **2**: BuLi (0.36 ml, 1.35 M in hexane) was added to a THF (1 ml) solution of diisopropylamine (75.8 μl, 0.54 mmol) at –45 °C and stirred for 10 min. The mixture was cooled to –78°C and a THF (1 ml) solution of **2** (78 mg, 0.16 mmol) was added dropwise *via* a syringe while maintaining the temperature below –70°C. The reaction mixture was stirred for 15 min and then treated with CH_3OD (67 μl, 1.64 mmol). After being quenched with AcOH (31 μl, 0.54 mmol), the mixture was allowed to warm to room temperature and partitioned between EtOAc (30 ml) and saturated aqueous $NaHCO_3$ (1 ml). The organic layer was washed with water (1 ml) and then with brine (5ml), and dried (Na_2SO_4). Evaporation of the solvent followed by column chromatography (10~25% EtOAc/hexane) gave **5** (22 mg, 33%) and **2** (17 mg, 25%). D-incorporation of the resulting **5** was calculated from its ^{1}H-NMR spectrum measured in $CDCl_3$.

1-(3,5-Bis-*O*-TBDMS-2-deoxy-D-*erythro*-pent-1-enofuranosyl)uracil (5) This compound was obtained as a powder (mp 129.0-130.0 °C). *Anal.* Calcd for $C_{21}H_{38}O_5N_2Si_2$: C, 55.47; H, 8.42; N, 6.16. Found: C, 55.62; H, 8.68; N, 5.94. UV absorption in MeOH: max 275 nm (ε 18000), min 245 nm (ε 6300). ^{1}H-NMR ($CDCl_3$) δ: 0.06, 0.07, 0.10, and 0.11 (12H, each as s, SiMe), 0.88 and 0.89 (18H, each as s, SiBu-*t*), 3.65 (1H, dd, *J*= 5.9 and 10.6 Hz, H-5'), 3.74 (1H, dd, *J*= 5.9 and 10.6 Hz, H-5'), 4.41 (1H, dt, *J*= 2.9 and 5.9 Hz, H-4'), 5.02 (1H, t, *J*= 2.9 Hz, H-3'), 5.55 (1H, d, J= 2.9 Hz, H-2'), 5.77 (1H, d, J= 8.4 Hz, H-5), 7.75 (1H, d, *J*= 8.4 Hz, H-6), 8.33 (1H, br, NH). MS *m*/*z*: 398 (M^+–Bu-*t*+1), 368 (M^+–Bu-*t*–2Me+H), 265 (M^+–TBDMSOH).

5'-*O*-TBDMS-2'-deoxy-2'-fluorouridine (6) TBDMSCl (800 mg, 5.3 mmol) was added to an ice-cooled solution of **1** (1.09 g, 4.4 mmol) and imidazole (722 mg, 10.6 mmol) in DMF (10 ml). The mixture was allowed to warm slowly to room temperature and stirred for 3 h. After being diluted with EtOAc (200 ml), the reaction mixture was washed with water (50 ml) and then with brine (50 ml). The organic layer separated was dried (Na_2SO_4), evaporated, and chromatographed on a silica gel column (25~33% EtOAc/hexane). This afforded 62 mg (3%) of **2** and 1.45 g (91%, as a foam) of **6**. *Anal.* Calcd for $C_{15}H_{25}FN_2O_5Si$: C, 49.98; H, 6.99; F, 5.27; N, 7.77. Found: C, 49.79; H, 7.03; F, 5.18; N, 7.64. UV absorption in MeOH: max 259 nm (ε 10800), min 228 nm (ε 3100). ^{1}H NMR ($CDCl_3$) δ: 0.13 (6H, s, SiMe), 0.93 (9H, s, SiBu-*t*), 2.50 (1H, br, 3'-OH), 3.87 (1H, dd, *J*= 2.2 and 12.1 Hz, H-5'), 4.06~4.14 (2H, m, H-4' and H-5'), 4.35 (1H, ddd, *J*= 4.4, 7.0, and 18.3 Hz, H-3'), 4.96 (1H, ddd, *J*= 1.8, 4.4, and 52.4 Hz, H-2'), 5.69 (1H, d, *J*= 8.1 Hz, H-5), 6.11 (1H, dd, *J*= 1.8 and 15.4 Hz, H-1'), 7.94 (1H, d, *J*= 8.1 Hz, H-6), 8.87 (1H, br, NH). MS *m*/*z*: 361 (M^++H), 303 (M^+–Bu-*t*), 283 (M^+–Bu-*t*–HF).

1-(3,5-Bis-*O*-TBDMS-2-trimethylsilyl-D-*erythro*-pent-1-enofuranosyl)-5-trimethylsilyluracil (9) BuLi (1.74 ml, 1.43 M in hexane) was added to a THF (7 ml) solution of 2,2,6,6-tetramethylpiperidine (0.48 ml, 2.8 mmol) at –30 °C. The mixture was stirred for 10 min and cooled to –78 °C, whereupon TMSCl (0.9 ml, 7.1 mmol) was added. A solution of **8** (322 mg, 0.71 mmol) in THF (7 ml) were added dropwise to the above mixture. The reaction mixture was stirred for 1 h at –78 °C, diluted with ether (30 ml), and treated with saturated aqueous $NaHCO_3$. The ether layer was partitioned between EtOAc (50 ml) and water (20 ml). The organic layer separated was washed with brine (50 ml) and dried (Na_2SO_4). Evaporation of the solvents followed by column chromatography (12.5% EtOAc/hexane) afforded 318 mg (77%) of **9** as a colourless oil. UV absorption in MeOH: max 257 nm, min 237 nm. ^{1}H-NMR ($CDCl_3$) δ: 0.09, 0.13, and 0.15 (21H, each as s, SiMe), 0.25 (9H, s, 5-$SiMe_3$), 0.91 (18H, s, SiBu-*t*), 3,61 (1H, dd, *J*= 7.0 and 10.5 Hz, H-5'), 3.79 (1H, dd, *J*= 5.1 and 10.5 Hz, H-5'), 4.39 (1H, ddd, *J*= 2.0, 5.1, and 7.0 Hz, H-4'), 5.01 (1H, d, *J*= 2.2 Hz, H-3'), 7.04 (1H, s, H-6), 8.20 (1H, br, NH). MS *m*/*z*: 584 (M$^+$–Me), 541 (M$^+$–Bu-*t*–H), 511 (M$^+$–Bu-*t*–2Me–H), 169 (B–Me+H).

MCPBA oxidation of compound 9 Compound **9** (54 mg, 0.09 mmol) was dissolved in dry CH_2Cl_2 (3 ml) and cooled to 0 °C. MCPBA (22 mg, 0.09 mmol) was added with stirring and the mixture was allowed to warm slowly to room temperature. After 3 h, the mixture was diluted with EtOAc (20 ml) and washed with 0.1*N* $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, water, and brine (5 ml each), successively. The organic layer was dried (Na_2SO_4) and filtered. Evaporation of the solvent followed by column chromatography (10% EtOAc/hexane) gave 35 mg (64%) of **10** as a solid. Crystallization from EtOAc-hexane gave an analytical sample (mp 130.0-130.5 °C). *Anal.* Calcd for $C_{27}H_{54}N_2O_6Si_4$: C, 52.72; H, 8.85; N, 4.55. Found: C, 52.99; H, 9.10; N, 4.45. UV absorption in MeOH: max 255 nm (ε 9700), min 229 nm (ε 6000). ^{1}H-NMR ($CDCl_3$) δ: 0.07, 0.08, 0.10, 0.13, and 0.16 (21H, each as s, SiMe), 0.23 (9H, s, 5-$SiMe_3$), 0.91 and 0.94 (18H, each as s, SiBu-*t*), 3.59 (1H, dd, *J*= 7.0 and 10.5 Hz, H-5'), 3.68 (1H, dd, *J*= 7.0 and 10.5 Hz, H-5'), 4.31 (1H, brt, *J*= 7.0 Hz, H-4'), 4.38 (1H, s, H-3'), 7.16 (1H, s, H-6), 7.93 (1H, br, NH). ^{13}C-NMR ($CDCl_3$) δ: –5.30, –5.20, –4.37, –4.02, –2.59, –1.83 (SiMe), 17.95 and 18.55 (each as s, Si*C*Me_3), 25.90 and 26.05 (SiC*Me*$_3$), 65.67 (t, C-5'), 70.48 (s, C-2'), 76.05 (d, C-3'), 89.20 (d, C-4'), 98.89 (s, C-1'), 111.11 (s, C-5), 144.56 (d, C-6), 148.77 (s, C-2), 165.10 (s, C-4). MS *m*/*z*: 614 (M$^+$), 599 (M$^+$–Me), 557 (M$^+$–Bu-*t*), 425 (M$^+$–Bu-*t*–TBDMSOH), 168 (B–Me).

X-ray crystallography of 10 The crystallographic data were collected on a Rigaku AFC-5 diffractometer using graphite monochromated $CuK\alpha_1$ radiation by ω–2θ scan method. The scan speed was 16 ° min^{-1}. The data were corrected for Lorentz and polarization factors, but no absorption correction was applied. A total of 1969 reflections were measured within the 2θ angle of 120 °. The crystal structure was determined by the direct method and refined by the full-matrix least-squares. The final R value was 0.075 for 1759 reflections above $3\sigma(F)$ including anisotropic thermal factors for non-hydrogen atoms and isotropic factors for hydrogen atoms.

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15) The isomeric 2',6-bis-TMS derivative was also formed in 7% yield.

16) Neither TMSCl alone nor TMSCl/2,2,6,6-tetramethylpiperidine effected C-2' silylation of **5** (in THF, below -70 °C).

17) Crystal data of **10** are as follows: space group $P2_1$ (monoclinic), $Z = 2$, $a = 19.552(5)$, $b = 7.231(2)$, $c = 13.388(1)$ Å, $\beta = 99.52(1)$ °, $V = 1866.9(8)$ Å^3, $D_c = 1.094$ gcm^{-3}.

18) In addition to **10**, an unstable product was detected by TLC, which decomposed on attempted purification by silica gel column chromatography.

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